

# Clinical Characteristics of Severe Covid Pneumonia: Exploring New Trends in ICU

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## Research

**Keywords:** Intensive care unit (ICU), SOFA, D-Dimers, APACHI II, SAPS II, Neutrophil to Lymphocyte ratio, Mortality

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# Abstract

**Background:** In late December 2019, Covid-19 emerged as clusters of pneumonia of unknown cause in a province of china, Wuhan. Etiological agent was identified as novel coronavirus that resembles severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory syndrome coronavirus (MERS-CoV) and has zoonotic transmission. Covid pneumonia can remain asymptomatic, present as mild infection, severe pneumonia or respiratory failure. Diagnosis is based on rRT-PCR carried out on respiratory secretions. Covid related mortality exceeds 50% once patient requires ICU admission.

**Objective:** To study the characteristics of ICU population admitted to ICU of Shifa International hospital.

**Results:** we prospectively analysed 74 patients which included 43.3% females and 56.7% males. Commonest symptoms were shortness of breath (94.5%), fever (74.3%) and cough (74.3%). Most of our study population consisted of non-smokers (79.7%) and had hypertension (59.4%) followed by diabetes (47.2%). Hydroxychloroquine (HCQ) and azithromycin combination is superior to hydroxychloroquine and doxycycline in reducing mortality ( $p=0.023$ ) whereas Doxycycline alone resulted in increased mortality ( $p=0.009$ ). Those who did not require antibiotics or required only narrow spectrum antibiotics had increased survival and reduced requirement of invasive mechanical ventilation ( $p< 0.0001$ ). in our study population, (44.9%) developed acute kidney injury, 2.7% needed re-intubations 10.8% developed surgical emphysema and 2.7 % thromboembolic events despite full anticoagulation. ICU mortality was 41.8% and was higher in females (59.4%,  $p=0.008$ ), those who had SOFA score  $> 3.5$  at time of admission, raised D-Dimers  $> 931$  ng/ml, NLR  $> 9.2$ . It was further high in those who required invasive mechanical ventilation and vasopressor support (58.1% mortality  $p< 0.001$ ). ICU stay was more prolonged in those requiring invasive mechanical ventilation as compared to those who did not. (23 days vs 6 days,  $p=0.001$ ). Mean plateau pressure was  $19.6 \pm 7.6$ ; mean Driving pressures  $14.4 \pm 4.6$ ; mean PaO<sub>2</sub>/FiO<sub>2</sub>  $150.7 \pm 73.9$ ; mean SPO<sub>2</sub>/FiO<sub>2</sub>  $173.9 \pm 106.9$ ; mean PEEP was  $8.2 \pm 4.33$ .

**Conclusion:** We concluded that severe covid pneumonia is common amongst males, non-smokers those who had comorbid. HCQ and azithromycin combination is superior to combination of HCQ and doxycycline or doxycycline alone and QT prolongation is a rare complication. Baseline NLR, APACHI II, SOFA, SAPS II, NUTRIC scores, D-Dimers, invasive ventilation and vasopressor support are important tools to predict ICU mortality. Invasive mechanical ventilation carries higher mortality and associated with more prolonged ICU stay. AKI is most common complication followed by shock and surgical emphysema. CRP, Ferritin levels has no impact on outcome.

## Introduction

Coronavirus disease 2019 is an emergent disease which manifested as clusters of undisclosed viral pneumonia in Wuhan, province of china in early decemebr 2019. Soon, chinese scientists unrevealed that etioloigcal agent is single stranded RNA novel coronavirus (1), now called covid-19, which closely resembles severe acure respiratory syndroms corona virus (SARS-CoV) and Middle East Respiratory

syndrome (MERS-CoV) (2). spread of infection was so rapid that an alarm was sent to WHO by chinese centre of disease control which declared it as pandemic in the end of January 2020(3). Vigorous epidemiological investigations found that it has probably zoonotic transmission (4) and has high human-to-human transmission through contact as well as droplets (5).

Clinical presentation of Covid-19 is quite diverse because its clinical spectrum extends from asymptomatic cases to mild infection (81%) and from severe pneumonia (14%) to respiratory failure requiring critical care (5%)(6). Diagnosis is confirmed by running RT-PCR on respiratory specimens either nasopharyngeal or throat swab. Respiratory failure is the leading cause of admission of ICU which is due to ARDS(7), thrombotic complications like pulmonary embolism (8) or haemoglobin abnormalities(9). Mortality in ICU patients is quite high and reported 62% in Wuhan and 52% in Washington, DC, USA (10). Given novelty of the disease, we present our clinical experience of treating Covid patients needing ICU care.

## **Material And Methods**

### **Objective:**

To study clinical characteristics of Covid pneumonia requiring ICU care.

### **Methodology:**

After IRB approval, we enrolled total 45 patients in our study. Informed consent was taken preferably from the patients or their surrogates. All authors adhered to the study protocol and reviewed the codex before submission. All patients admitted to ICU from Emergency Room (ER) or admitted from floor with respiratory failure with established diagnosis of Covid Pneumonia on RT-PCR run on respiratory specimen. Patients who were initially admitted with respiratory failure and their awaited RT-PCR results came negative, were excluded from the study. History was taken on phone or from the surrogate accompanying the patient. physical examination was performed by fellow ICU within 1st hour of presentation. Fever was recorded as axillary temperature  $> 100^{\circ}$  F, lymphopenia  $< 1000$  cells per cubic millimeter, thrombocytopenia as  $< 150000$  cells per cubic millimeter, deranged Liver function test as serum bilirubin  $> 1.1$  mg/dl or ALT  $> 40$  IU/ml and acute kidney injury as serum creatinin  $> 1.1$  mg/dl. All patients received Zinc 60 mg once daily per oral, methylprednisolone 40 mg twice daily, thiamine 200 mg once daily intravenous and vitamin C in oral form once daily. All those who required vasopressors or invasive mechanical ventilation were passed central venous catheter and arterial line. If any patient had 2 consecutive RT-PCR of respiratory specimens negative, was considered negative for covid and transferred to high dependency unit or non-covid area. Primary outcome was discharge from ICU or death of the patient.

### **Characteristics of ICU population:**

Data was collected on a preformed structured questionnaire by an ICU specialist. Demographic data, symptomatology and Co-morbidities were recorded. All labs were conducted from Shifa laboratories. HRCT chest and chest X-rays were performed at radiology department. Clinical scores like APACHE II, SOFA, NUTRIC and SAPS II were calculated using online MDcalc calculator. Respiratory devices, oxygen requirements, ventilator settings, arterial blood gases, PaO<sub>2</sub>/FiO<sub>2</sub> were recorded by respiratory therapist and verified by the ICU specialist.

### **Statistical Analysis:**

Prior sample size was not calculated, and it was equal to the number of patients treated from March to May. 31<sup>st</sup> May was the final follow up date. Analysis was done using SPSS 21. Continuous variables were tested for normality by Shapiro-wilk test and presented in median and Inter-quartile range (IQR). Patients were divided into 3 categories according to age; < 40; 40-50; 51-60; > 60. Chi-square test was applied for categorical variables and t-test was applied to test means with categorical variables. Statistical significance was defined as  $p < 0.05$ .

## **Results**

We present prospective analysis of 74 patients of which 43.3% were females and 56.7% were males. Shortness of breath was the most common symptom (94.5%) trailed by fever (74.3%) and cough (74.3%). Amongst rare presentations, one patient had acute limb ischemia and one had stroke at time of presentation. We observed majority of the patients were non-smokers (79.7% vs 20.30%); need for invasive mechanical ventilation and mortality was high in clusters of smokers though statistically it did not reach level of significance (46.7% vs 42.7%, 46.7% vs 40.7%  $p = 0.77, 0.77$  respectively). Most of the patients had hypertension (59.4%) followed by diabetes (47.2%), post liver transplant (2.7%). Calculated mortality scores like APACHE II median 14 (IQR 10–20); SOFA median 4 (IQR 3–6); SAPS II median 33 (IQR 022–44); NUTRIC 3 (IQR 2–5) were of significance as median values of SAPS II and NUTRIC score calculated at time of presentation to ICU, (33.0 and 3.0 respectively) strongly predicted ICU mortality (CI 95%,  $p = 0.013$  and  $0.038$  respectively) (see table of predictors below). Median values of CRP, D-Dimers and serum Ferritin on admission to ICU were 115.5 (IQR 71.2-240.5), 1153 (IQR 396.5–4021), 1217 (IQR 593–1979 respectively). Solely, a pair of patients (2.7%) developed prolonged QT interval during treatment with HCQ and azithromycin; however, median values of QT interval on presentation and subsequent values over 5 days remained traditional (see table). Twenty-three 23 (31.0%) patients were treated with combination of hydroxychloroquine (HCQ) and azithromycin; 21 (28.3%) with doxycycline alone; 29 (39.1%) with HCQ and doxycycline; HCQ & Azithromycin was significantly associated with reduction of mortality ( $p = 0.023$ ) whereas mortality was high in doxycycline group. ( $p = 0.009$ ); however, doxycycline reduced ICU stay (mean 5.2 (1–18)  $p = 0.002$ ). Antifungals were given in (11/74 13%) patients for fungal co-infections or occult fungemia. We observed 17 of our patients who were given no antibiotics ( $n = 7$ ) or narrow spectrum antibiotics ( $n = 10$ ) had better survival outcome (14 survivors, 3 non-survivors, CI 95%,  $p = 0.026$ ) and reduced requirement of mechanical ventilation (none of our study population required IMV, CI 95%,  $p = < 0.0001$ ) as compared to those who required empirical or culture and sensitivity guided broad

spectrum antibiotics for bacterial co-infections (29 survivors vs 28 survivors, 32 required IMV, and 25 did not require IMV). Secondary bacterial infections have been uncommon in our study population (2.7% in central venous lines vs 10.8% in blood cultures vs 13% in tracheal cultures). During treatment, 32 patients (43.2%) required invasive mechanical ventilation and 27 of them (84.3%) deteriorated from Non-invasive ventilation to mechanical ventilation during treatment. There was no survival benefit in early intubations (n = 24) (32.4%) as compared to late intubations (n = 8) (10.8%) this may be due to unequal arms. Mean plateau pressure was  $19.6 \pm 7.6$ ; mean Driving pressures  $14.4 \pm 4.6$ ; mean PaO<sub>2</sub>/FiO<sub>2</sub>  $150.7 \pm 73.9$ ; mean SPO<sub>2</sub>/FiO<sub>2</sub>  $173.9 \pm 106.9$ ; mean PEEP was  $8.2 \pm 4.33$ . Two of our patients (2.7%) needed re-intubations; 8 (10.8%) developed surgical emphysema and out of them 3 (4%) had to undergo tube thoracotomy during invasive mechanical ventilation. Tracheostomy was required in 2 (27%) of our patients in order to wean them off ventilator and both did not survive. In our study cohort, 42 (56.7%) patients did not require intubation and were managed with either non-rebreather mask, non-invasive ventilation or high flow nasal cannula (HFNC).

A large percentage of our study population (32/74, 44.9%) experienced acute kidney injury (AKI) during ICU stay. Multiple comorbid (23/32, 71.9% p = 0.005), hypertension (21/32, 65.6% p = 0.04), invasive mechanical ventilation (19/32 59.4% p = 0.04), vasopressors support (16/32, 50% p = 0.004) were strong predictors of development of AKI; whereas, AKI was also common in male gender (18/32, 56.2%), older age group > 60 years (19/32 59.4%) and diabetics (18/32, 56.2%). Only (2.7%) required intermittent haemodialysis and 3 (4.0%) of them required continuous renal replacement therapy. Our results did not establish any statistically significant relationship between development of acute kidney injury and outcome (p = 0.173). As suggested by autopsy findings of 12 Covid patients that there is high risk of thromboembolic events we offered anticoagulation to 64 patients based on D-Dimer values, prophylactic anticoagulation was given to 7 patients only and 57 were given full anticoagulation and found that there is no statistically significant relationship between therapeutic anticoagulation and mortality (CI 95%, p = 0.014). None of our patients developed pulmonary embolism or deep venous thrombosis. Two of our patients (2.7%) developed stroke on prophylactic dose of anticoagulation.

ICU mortality remained high in our study population 31 out of 74 (41.8%) and was statistically significant amongst females (59.4% vs 28.6% CI 95% p = 0.008). Mortality was further increased in clusters requiring invasive mechanical ventilation as compared to those who did not require invasive mechanical ventilation (68.8% vs 21.4% CI 95% p = < 0.001). NLR, SOFA score at presentation and baseline D-dimers > 1391 ng/dl were predictors of requirement of mechanical ventilation (CI 95% 0.024 vs 0.044 vs 0.014 respectively); Median values of NLR (9.22) was also predictor of requirement of invasive mechanical ventilation (CI 95%, p = 0.046%). Similarly, Age, baseline values of CRP, d-dimers, LDH and serum ferritin and SOFA score could not reach to statistically significant level as predictors of mortality. Similarly, Age, diabetes, hypertension, multiple comorbid and lymphopenia were poor predictors of requirement of vasopressors or invasive mechanical ventilation (CI 95% p = > 0.05). Twenty-three (23, 31.0%) required vasopressors during ICU course and 18 of them (58.1% vs) could not survive. Requirement of vasopressors was a strong predictor of mortality (CI 95%, p = < 0.001). Requirement of vasopressors was high amongst elderly patients above 60 years of age, diabetics and lymphopenic patients (41%, 40%.

41%, CI 95% p = 0.021, 0.137-0.078 respectively). Invasive mechanical ventilation also prolonged ICU stay as shown by Kaplan-Meier survival scale; those who did not require invasive mechanical ventilation had an ICU stay of 6 days (lower bound 3.7; upper bound 8.2) as compared to 23 days (lower bound 19.1; upper bound 26.8) for those who required invasive mechanical ventilation. (CI 95% p = < 0.001) (See survival plot). Two of our patients who required invasive mechanical ventilation for typical ARDS had prolonged hospital stay (65 days and 49 days) and both became dependent on non-invasive mechanical ventilation. Female gender, baseline APACHI II > 14; SAPS II > 33; NUTRIC > 3.5; SOFA score > 3.5; NLR > 9.6; D-Dimers > 930.5 ng/ml; Ferritin levels > 837 ng/ml at baseline predicts ICU mortality.

## Discussion

After careful and thorough search on PubMed, and to the best of our knowledge, this is largest case study of 74 patients admitted to ICU of a single centre. Shortness of breath, fever and cough were the most common symptoms; elderly people, multiple comorbid, hypertension and diabetes were most important comorbid. This pattern is in line with studies from china and United States (6, 11, 12). Smokers were less (20.3%) in our study population. And our findings are supported by Zhang et al. and Guan et al who reported 1.4% and 12.6% smokers in their study population respectively (13, 14). A systematic review done by Vardavas et al (15) reported disease progression is more rapid and more severe in smokers. SAPS II  $\geq$  33 and Nutric score  $\geq$  3 calculated at time of presentation to ICU predicts mortality. Combination of HCQ and azithromycin reduced mortality as compared to the combination of HCQ and doxycycline or doxycycline alone; however, none of these regimens decreased ventilator requirement. Use of HCQ and azithromycin was supported by a French open label non randomized trial of 42 patients who gave HCQ and azithromycin to 26 patients and found synergistic phenomenon interplaying between two drugs that could create statistically significant difference in viral clearance (16); however, subsequent studies from united states did not prove any clinical mortality benefit of using combination of HCQ and azithromycin(17). Secondary bacterial infection was far less common and it may be attributable to contact and airborne precautions taken by the nursing staff and reduced exposure to the visitors. Those who required broad spectrum antibiotics are more likely to require invasive mechanical ventilation and carried poor outcome. This effect may be due to antibiotic related inflammatory storm as few antibiotics may stimulate immune system to release IL-6 and TNF- $\alpha$  (18). Acute kidney injury was the most common complication in our population (44.9%). Our reported incidence of AKI and risk factors are more or less same as evaluated in previous meta-analysis (19). Surgical emphysema and pneumomediastinum was frequent complication as mentioned in a case series (20); however, Re-intubations, tube thoracotomy and thrombotic complications had been rare in our study population. ICU mortality was quite higher (41.8%) in our study population and even higher in those who required invasive mechanical ventilation eventually (68.8%) and statistically significant predictor of ICU mortality. Our mortality score was less than reported in a case series of 24 patients from USA (50%) and in comparison to their vented population (75%), 43.2% of our study population required invasive mechanical ventilation (21). Another multicentre study of 1591 ICU populace mentioned 26% mortality and 88% received invasive mechanical ventilation (22). These results contrast with our study where we observed more mortality in invasive mechanical ventilation.

SOFA Score calculated at admission to ICU and increasing D-Dimers, NLR at baseline and vasopressor support predicted requirement of invasive mechanical ventilation and ICU mortality as identified in previous studies (23–25). In addition to this, our results explored that female gender, baseline APACHI II, SAPS II, NUTRIC scores were also predictors of ICU mortality.

## Conclusion

We concluded that severe covid pneumonia is common amongst males, non-smokers those who had comorbid. HCQ and azithromycin combination is superior to combination of HCQ and doxycycline or doxycycline alone and QT prolongation is a rare complication. Baseline NLR, APACHI II, SOFA, SAPS II, NUTRIC scores, D-Dimers, invasive ventilation and vasopressor support are important tools to predict ICU mortality. NIV has survival benefit and decreases hospital stay. Invasive mechanical ventilation is associated with increased mortality, more prolonged hospital stay.

## Recommendations

Based on our results, we recommend that broad spectrum antibiotics should be avoided and used only if there is strong clinical indication. Clinical scoring and baseline D-Dimers, Ferritin and NLR may guide ICU physicians to decide limits of care with surrogates, reduce the need of invasive mechanical ventilation and help in addressing expanding utilization of ICU resources.

## Abbreviations

AKI Acute kidney injury

APACHI II Acute Physiology And Chronic Health Evaluation

ARDS Acute respiratory distress syndrome

CKD Chronic kidney disease

CRP C-Reactive protein

HCQ Hydroxychloroquine

HFNC High flow nasal cannula

ICU Intensive care unit

IL-6 Interleukin-6

LDH Lactate dehydrogenase

NLR Neutrophil to lymphocyte ratio

PEEP Positive end expiratory pressure

SOFA sequential organ failure assessment score

SAPS II Simplified Acute Physiology Score II

TNF Tumor necrosis factor

## **Declarations**

### **Ethics approval and consent to participate:**

Informed consent was taken from all participants and study was approved from IRB of Shifa international hospital Islamabad

### **Consent for publication:**

Manuscript does not contain any individual person's data

### **Availability of data and material:**

Will be uploaded on mentioned repositories

### **Funding:**

No funding was received from any funding body

### **Competing interests:**

There are no financial or non-financial competing interests.

### **Author's contributions:**

Each author's contributions are given in table followed by title.

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## Tables

Table 1  
Demographic, and clinical data

<b>Demographics</b>		
Age		
mean (SD)	60.9 (11.7)	
Median	61.5	
<b>Gender</b>		
Male	42	56.70%
Female	32	43.20%
<b>Medical History</b>		
Non-smoker	59	79.70%
Smokers	15	20.20%
Fever		
< 100	19	25.60%
> 100	55	74.30%
Cough		
Absent	19	25.60%
Present	55	74.30%
Dyspnea		
Absent	4	5.40%
Present	70	94.50%
Diabetes	35	47.2%
Hypertension	44	59.4%
Ischemic Heart disease	15	20.2%
CKD	11	14.86%
Malignancy	2	0.2.7%
Cirrhosis (status post liver transplant)	2	2.7%
CVA	1	1.30%

**HOSPITAL COURSE:**

<b>Demographics</b>		
Multiple co-morbids	41	55.40%
Others	4	5.40%
<b>On Presentation</b>		
APACHI II		
Mean (SD) 16	16 (7.61)	
Median (IQR)	14 (10–20)	
SAPS II		
Mean (SD)	34 (14.5)	
Median (IQR)	33 (22–44)	
Nutric score		
Mean (SD)	3.7 (1.7)	
Median (IQR)	3 (2–5)	
SOFA score		
Mean (SD)	5.2 (3.46)	
Median (IQR)	4 (3–6)	
<b>Lab Data</b>		
CRP on day 1		
mean (SD)	145.9 (102.7)	
Median (IQR)	115.5(71.2-240.5)	
CRP on day 3		
mean (SD)	127.9 (98.5)	
Median (IQR)	93(51-177.7)	
CRP on day 5		
mean (SD)	85.7 (81.9)	
Median (IQR)	59.5 (21.3-122.5)	
CRP on day 7		
mean (SD)	51.2 (67.5)	
<b>HOSPITAL COURSE:</b>		

<b>Demographics</b>	
Median (IQR)	24.5 (7.2–75.2)
Procalcitonin	
Day 1	
mean (SD)	5.78 (19.6)
Median (IQR)	0.54 (0.26–1.90)
Day 3	
Mean (SD)	1.27 (1.9)
Median (IQR)	0.66 (0.17–1.24)
Day 5	
Mean (SD)	1.98 (5.26)
Median (IQR)	0.17 (0.77 – 0.76)
Day 7	
Mean (SD)	0.57 (1.14)
Median (IQR)	0.16 (0.07–0.44)
QT on day 1	
mean (SD)	404.8 (18.6)
Median (IQR)	405 (394–420)
QT on day 2	
mean (SD)	409 (19.4)
Median	410 (400–420)
QT on day 3	
mean (SD)	411 (23.80)
median (IQR)	415 (400–422)
QT on day 4	
mean (SD)	416 (17.5)
Median (IQR)	415 (408–428)
QT on day 5	
<b>HOSPITAL COURSE:</b>	

<b>Demographics</b>	
mean (SD)	423.40 (23.2)
Median (IQR)	425 (409–440)
Ferritin on day 1	
mean (SD)	3112 (8990.3)
Median (IQR)	1217 (593–1979)
Ferritin on day 3	
mean (SD)	1558 (2192)
Median (IQR)	938 (551.7-1892.5)
Ferritin on day 5	
mean (SD)	1263.2 (957.6)
Median (IQR)	1002 (615-1495.2)
Ferritin on day 7	
mean (SD)	1065.6 (605.6)
Median (IQR)	973(629–1417)
D-Dimers on day 1	
mean (SD)	4219.4 (9724.1)
Median (IQR)	1153 (396.5–4021)
D-Dimers on day 3	
mean (SD)	2885.4 (3116.3)
Median (IQR)	1192 (511.5–4425)
D-Dimers on day 5	
mean (SD)	8345.3 (19436.7)
Median (IQR)	1928 (696–5156)
D-Dimers on day 7	
mean (SD)	7962.2 (17459.6)
Median (IQR)	1876 (1251.5-5747.7)
NLR	
<b>HOSPITAL COURSE:</b>	

<b>Demographics</b>	
mean (SD)	13.7 (11.2)
Median (IQR)	9.22 (6-18.45)
<b>ICU days</b>	
mean (SD)	9.12 (6.98)
median (IQR)	7 (3.75–12.25)
<b>Ventilator free days</b>	
mean (SD)	6.10 (4.83)
median (IQR)	5 (2–9)
<b>Days taken to progress to invasive mechanical ventilation</b>	
mean (SD)	3 (3.97)
median (IQR)	2 (0-5.5)
<b>Renal complications</b>	
No AKI	33/74 (44.5%)
AKI	32/74 (43.2%)
Already a case of CKD	9/74 (12.1%)
<b>Renal replacement therapy</b>	
Not required	64/74 (86.4%)
Required intermittent Hemodialysis	2/74 (2.7%)
CRRT	3/74 (4%)
Already dialysis dependent	9/74 (12.1%)
<b>Medications</b>	
HCQ	1/74 (1.3%)
HCQ & Azithromycin	23 (31%)
HCQ & Doxycycline	29 (39.1%)
Doxycycline	21 (28.3%)
<b>Antibiotics</b>	

**HOSPITAL COURSE:**

<b>Demographics</b>	
Narrow spectrum	10 (13.55%)
MRSA & ESBL	25 (33.7%)
Extended spectrum	31 (41.8%)
<b>CVC Cultures</b>	
No growth	72 (97.2%)
Acinetobacter	1 (1.3%)
Candida	0
Pseudomonas	1 (1.3%)
MRSA/ MSSA	0
Klebsiella	0
E.Coli	0
Enterococcus	0
<b>Blood cultures</b>	
No growth	66 (89.1%)
Acinetobacter	3 (4%)
Candida	1 (1.3%)
Pseudomonas	0
MRSA/ MSSA	0
Klebsiella	0
E.Coli	1 (1.3%)
Enterococcus	3 (4%)
<b>Tracheal cultures</b>	
No growth	63 (85.1%)
Acinetobacter	2 (2.7%)
Candida	5 (6.7%)
Pseudomonas	1 (1.3%)
MRSA	1 (1.3%)
<b>HOSPITAL COURSE:</b>	



<b>Demographics</b>	
Klebsiella	0
E.Coli	0
Enterococcus	2 (2.7%)
<b>Antifungals</b>	
No antifungals given	63 (85.1%)
Antifungals given	11 (14.8%)
<b>Invasive Mechanical ventiation</b>	
Required	32 (43.2%)
Not required	42 (56.7%)
<b>Non-invasive ventilation</b>	
Non-Rebreather Mask	15 (20.2%)
High flow nasal cannula	5 (6.7%)
Bipap/CPAP	24 (32.4%)
NIV to Mechanical Ventilation	27 (36.4%)
Received Intubated	3 (4%)
<b>Early vs Late intubation</b>	
Early intubation (Within 7 days)	24 (32.4%)
Late intubation (7 or above)	8 (10.8%)
<b>Re-Intubations</b>	2 (2.7%)
<b>Pneumomediastinum/Surgical emphysema</b>	9 (12.1%)
<b>Tube thoracostomy</b>	3 (4%)
<b>Vasopressor</b>	
Required	23 (31%)
Not required	51 (69%)
<b>Outcome</b>	
Survived	43 (58.1%)
Non-survived	31 (41.8%)
<b>HOSPITAL COURSE:</b>	

<b>Demographics</b>	
<b>Mean Plateau Pressure</b>	
Mean (SD)	19.6 (7.6)
Median (IQR)	20.1 (16.2–25.8)
<b>Mean Driving Pressure</b>	
Mean (SD)	14.4 (4.6)
Median (IQR)	15.5 (11–18)
<b>PaO2/FiO2 Ratio</b>	
Mean (SD)	150.7 (73.9)
Median (IQR)	130.3 (106.6-178.4)
<b>SPO2/FiO2 Ratio</b>	
Mean (SD)	173.9 (106.9)
Median (IQR)	128.6 (87.7-262.2)
<b>PEEP</b>	
Mean (SD)	8.2 (4.33)
Median (IQR)	6.9 (5.1–9.5)
<b>No. of days of Proning</b>	
Mean (SD)	2.4 (2.0)
Median (IQR)	2 (1-3.5)
<b>Stroke</b>	3 (4%)
<b>Left limb ischemia</b>	1 (1.3%)
<b>HOSPITAL COURSE:</b>	

Table 2  
PREDITORS OF MORTALITY

Predictor	Value	Sensitivity	Specificity	p value
APACHI II	14.5	64.5	67.4	0.007
SAPS II	32.5	71.0	60.5	0.001
NUTRIC	3.5	64.5	65.1	0.006
SOFA	3.5	87.1	44.2	0.027
NLR	9.6	63.3	69.8	0.01
FERRITIN	837	69.6	52.6	0.031
D-DIMERS	930.5	75.9	50	.009
Results shown in the table represent values recorded on admission to ICU. NLR (Neutrophil to lymphocyte ratio).				

Table 3  
ROLE OF HCQ AND AZITHROMYCIN VERSUS HCQ AND DOXYCYCLINE IN REDUCING ICU DAYS AND DAYS ON MECHANICAL VENTILATOR

Drugs	ICU days	Days on IMV
HCQ & Azithromycin upper bound- lower bound p value	Mean difference (-2) (-5.5-1.3 days) P = 0.235	Mean difference (-1.1) (-3.6-1.4 days) p = 0.395
HCQ & Doxycycline upper bound- lower bound p value	Mean difference (-2.4) (-5.5-0.8 days) p = 0.149	Mean difference (.05) (-2.3-2.4 days) p = 0.96
Doxycycline upper bound- lower bound p value	Mean difference (5.3) (1.9–8.7 days) P = 0.0026	Mean difference (1.5) (-1.5-4.1 days) p = 0.24
IMV stands for invasive mechanical ventilation		

Table 4  
DETERMINANTS OF INVASIVE MECHANICAL VENTILATION AND MORTALITY

	Requirement of IMV n = 32	non-survivors n = 31)	P value
Gender (male vs females)	17 (53.1%) ,15 (46.9%)	12 (38.7), 19 (61.3%)	0.64, 0.01
Age (51–60 vs > 60)	9 (28.1%), 19 (59.4%)	7 (30.4%), 20 (64.5%)	0.40, 0.168
Comorbid (0–1 vs > 1)	10 (31.2%), 22 (68.8%)	10 (32.3%), 21 (67.7%)	0.232, 0.240
Diabetes mellitus (yes vs no)	17 (53.1%), 15 (46.9%)	17 (54.8%), 14 (45.2%)	0.482, 0.347
Hypertension (yes vs no)	21 (65.6%), 11 (34.4)	21 (67.7%), 10 (32.3%)	0.474, 0.240
Non-smokers vs smokers	25 (78.1%), 7 (21.9%)	24 (77.4%), 7 (22.6%)	0.778, 0.772
IMV required vs not required		22 (71%), 9 (29%)	< 0.001
Acute kidney injury (yes vs no)	19 (59.4%), 11 (34.4%)	17 (54.8), 10 (32.3%)	0.042, 0.170
Anticoagulation (full vs partial)	28 (87.5%), 3 (9.4%)	27 (87.1%), 4 (12.9%)	0.07, 0.01
Early vs late intubation		16 (69.6%), 7 (30.4%)	0.382
Lymphocytes (yes vs no)	21 (65.6%), 11 (34.4%)	20 (64.5%), 11 (35.5%)	0.63, 0.10
Vasopressors	21 (65.6%), 11 (34.4%)	18 (58.1%), 13 (41.9%)	<0.001, < 0.001
	Requirement of IMV n = 32	non-survivors n = 31)	P value
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Vasopressors	21 (65.6%), 11 (34.4%)	18 (58.1%), 13 (41.9%)	<0.001, <0.001

## Figures

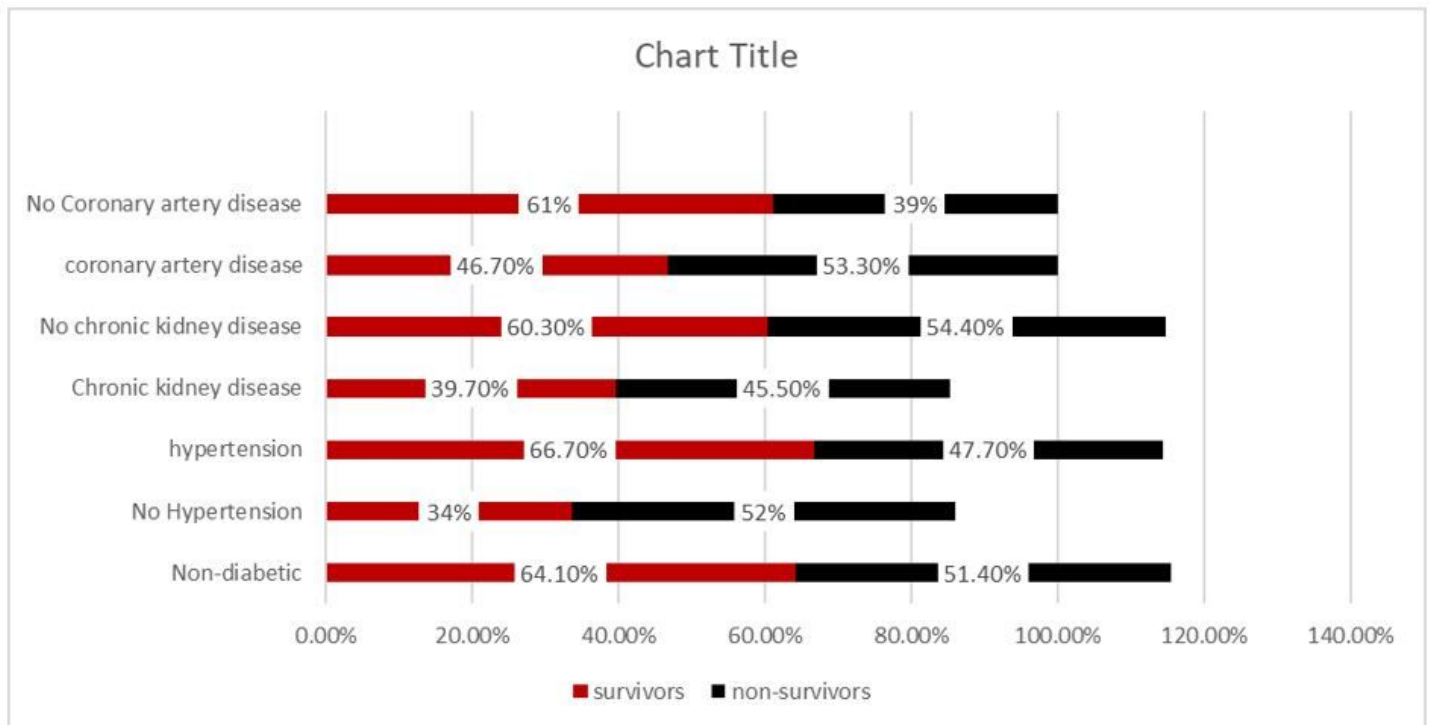


Figure 1

Comorbid and Outcome

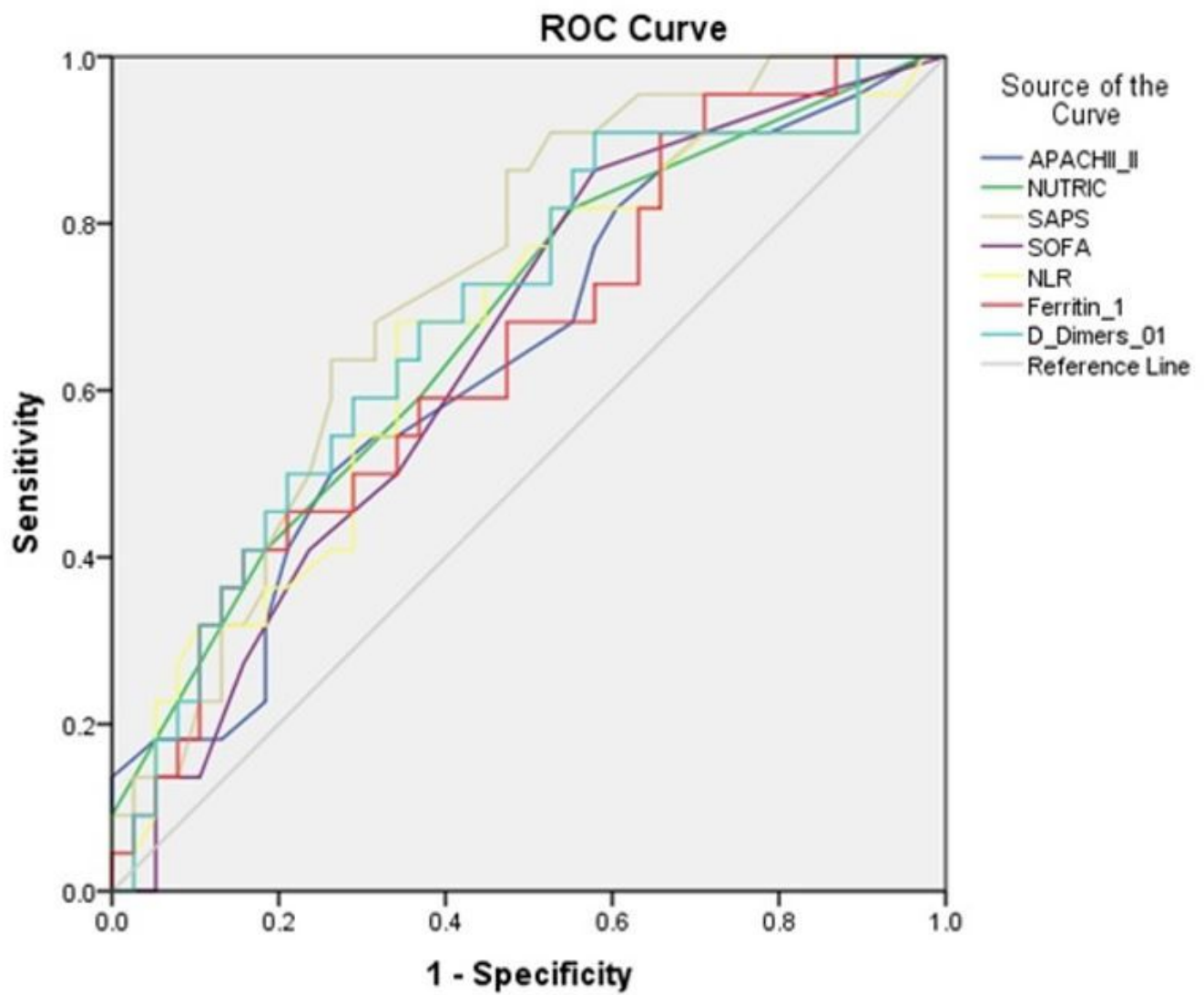
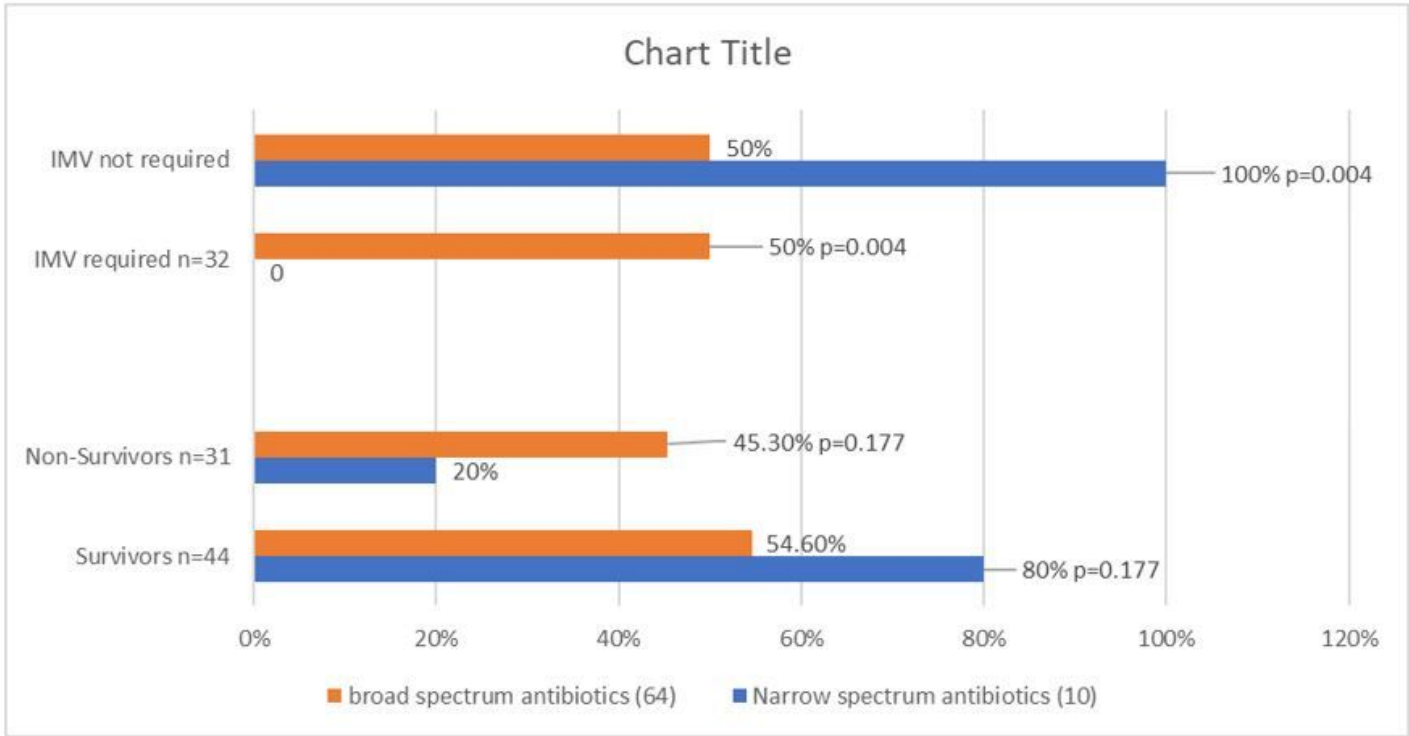


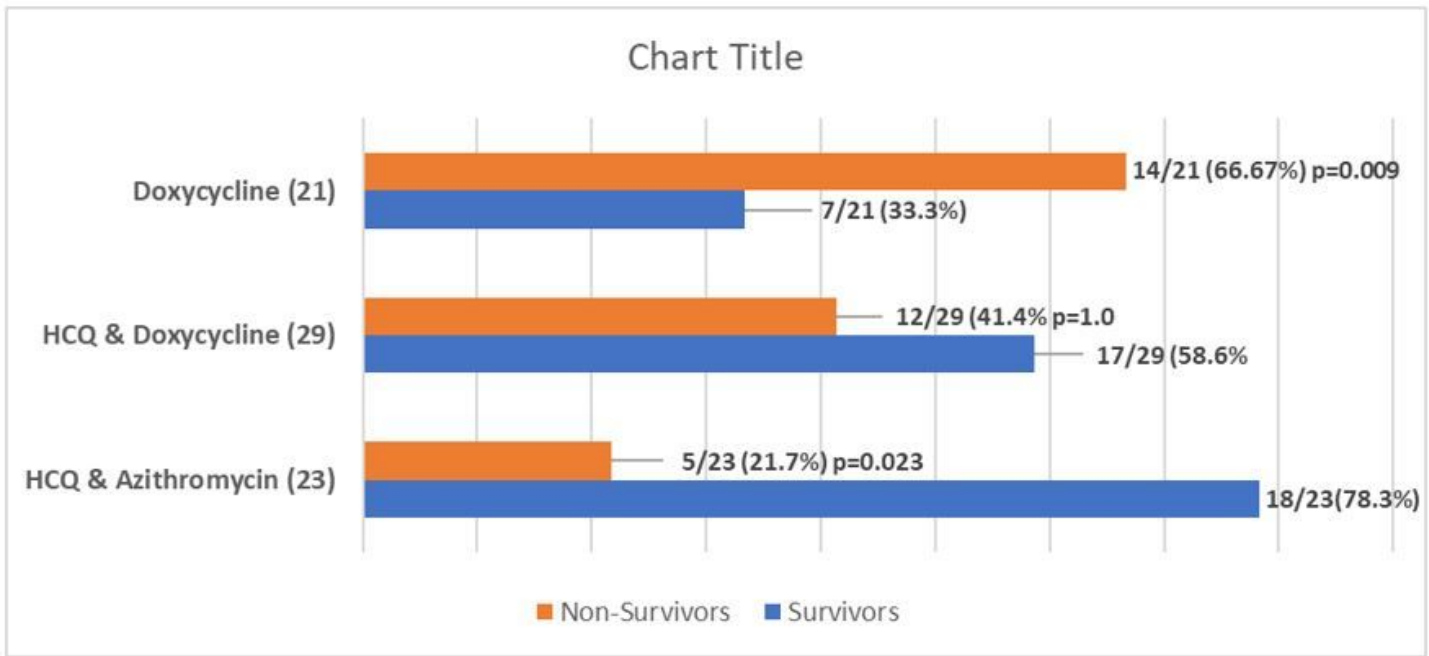
Figure 2

Sensitivities and Specificities Are Shown in Roc Curve



**Figure 3**

Relation of Antibiotics and Outcome and Requirement of Invasive Mechanical Ventilation



**Figure 4**

Role of Hcq and Azithromycin Versus Hcq and Doxycycline in Outcome

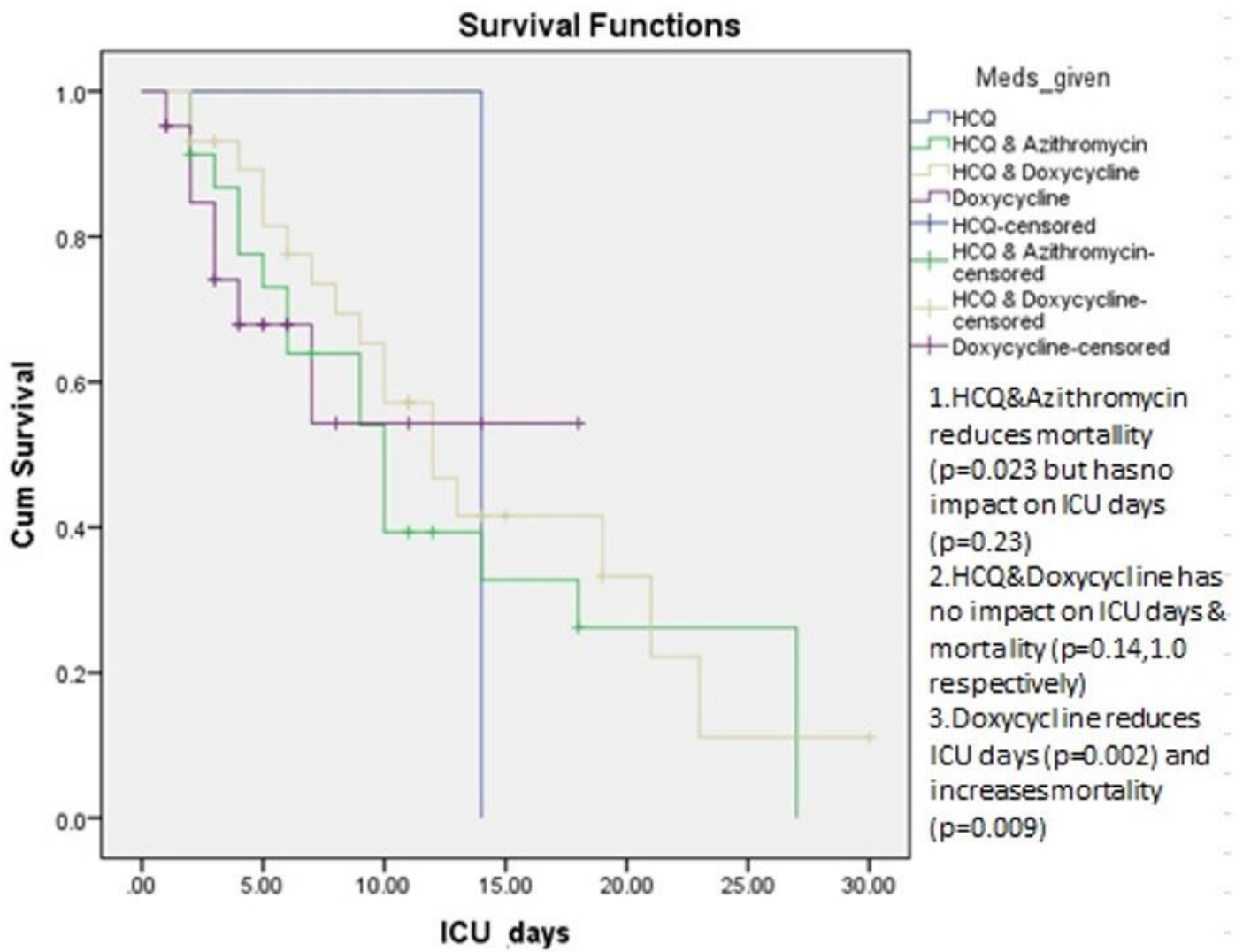
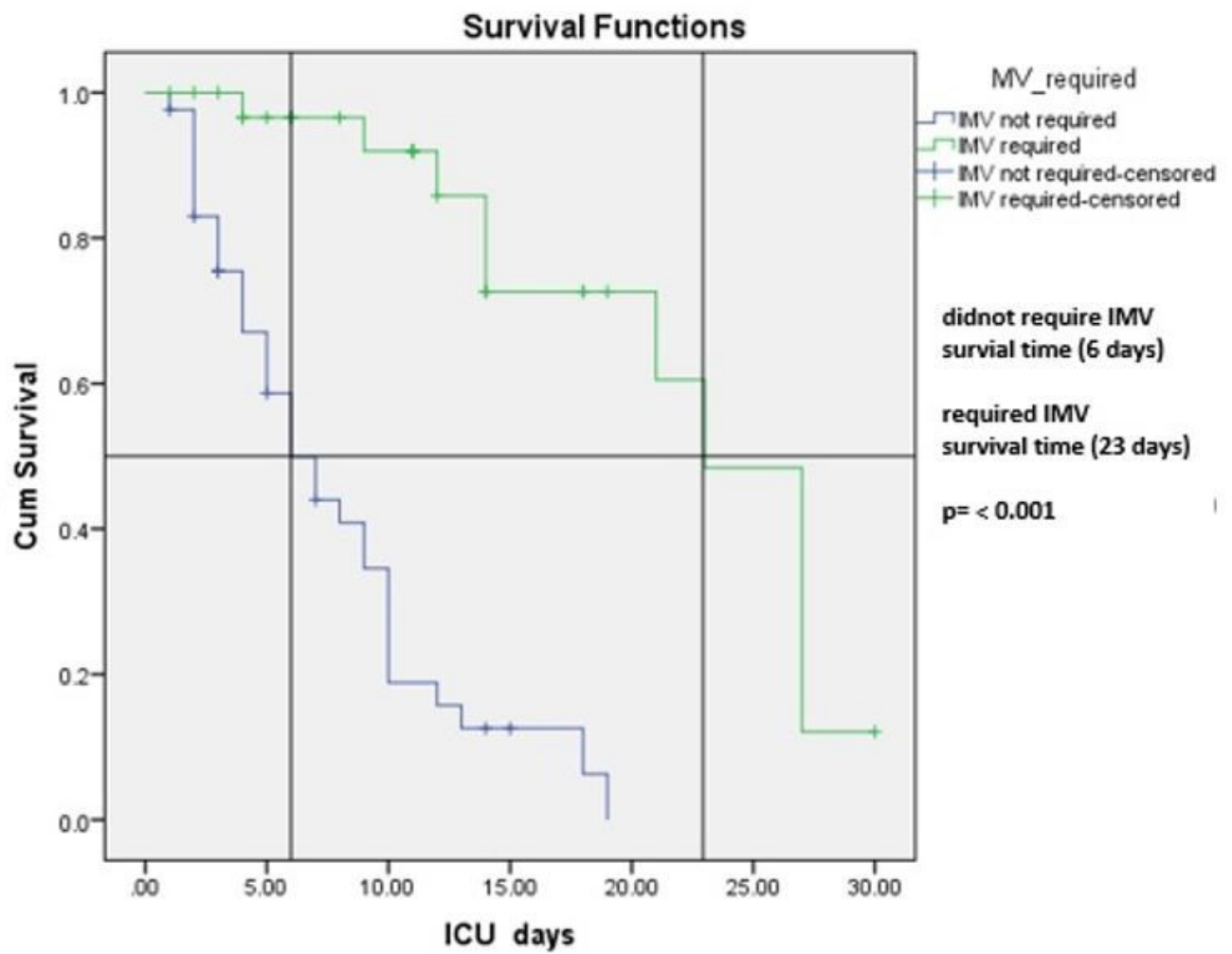


Figure 5

Survival Plot of Hcq and Azithromycin Vesus Hcq and Doxycycline and Doxycycline





**Figure 6**

Survival Plot of Invasive Mechanical Ventilation